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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 11/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/998,667	MASUDA ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) *17,18 and 20-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

It is noted that the instant application has been transferred to a new examiner. The application is now being examined by Examiner Richard Hutson in Art Unit 1652. Correspondence should be directed to Examiner Richard Hutson.

Claims 1-46 are still at issue and are present for examination.

Election/Restrictions

Applicant's election with traverse of Group II, Claims 1-16 and 19, drawn to a method for identifying a compound that modulates T lymphocyte activation, in vitro, wherein the compound is a small organic molecule, in the paper of 9/28/2004, is acknowledged. The traversal is on the ground(s) that Groups I-IV be examined together, as claim 1 is a genus claim to methods of identifying compounds that modulate T lymphocyte activation. Applicants further submit that groups V and IV(VI) be examined with groups I-IV. The basis for applicants request that groups V and VI be combined with the elected group III, is that all the required method steps in Groups V and VI are also found in elected Group III.

This argument is acknowledged, however, found nonpersuasive on the basis that both of groups V and VI require "determining the chemical or phenotypic effect of the compound upon a **cell** comprising the TRAC1 polypeptide". The elected group III is directed to methods comprising "determining the functional effect of the compound upon the TRAC1 **polypeptide**". Thus while groups V and VI are directed to determining the effect on a cell, elected group III is directed to determining the effect on a polypeptide

and thus all the required method steps of groups V and VI are **not** also found in elected group III.

Applicant's comments regarding claim 1's treatment as a linking claim are acknowledged.

Claim 1 link(s) inventions I through IV. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 1. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Thus based on the above, applicant's traversal of the restriction requirement is found nonpersuasive.

The requirement is still deemed proper and is therefore made FINAL.

Claims 17, 18, 20-46 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in the paper of 9/28/2004.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

There are currently no information disclosure statements in the instant application.

Specification

The disclosure is objected to because of the following informalities:

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth: The following portions of the specification list sequences which appear to meet the definition for a nucleic acid or amino acid sequence, but do not have an associated SEQ ID No: Figures 7,8 and 13. It is further noted that the corresponding sequence identifier for each of the sequences in a figure, must be listed either in the figure itself or in the description of the figure.

Appropriate correction is required.

Claim Objections

Claims 1 is objected to because of the following informalities:

Claims 1, part (ii) recites "determining the functional effect of the compound upon the TRAC1 polypeptide" wherein part (i) refers to a "TRAC1 polypeptide or a fragment thereof". It is suggested that applicants amend the claim to maintain consistency , such as amending part (ii) to read "determining the functional effect of the compound upon the TRAC1 polypeptide **or fragment thereof**"

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-16 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (2-16 and 19 dependent on) is indefinite in that it is unclear and confusing in the recitation "... determining the functional effect of the compound upon the TRAC1 polypeptide." Specifically it is unclear what applicants intend to be considered to be a "functional effect". These comments are made in light of applicants definition on page 10, lines 12-34, in which applicants state that essentially a "functional effect" is any parameter that is either indirectly or directly under the influence of a TRAC1 protein".

Claims 3, 4, 7, 8 and 12 are further indefinite in that it is unclear when the recited "functional effect" is a "chemical effect" and when it is a "physical effect".

It is noted that claim 5 which recites "the functional effect is determined by measuring ligase activity" is included in the rejection because it appears that it may be applicants intent that the functional effect is "the effect of ligase activity", it remains that the "functional effect" may include an effect beyond "ligase activity".

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 and 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-16 and 19 are directed to all possible methods comprising contacting a compound (any small organic) with any "TRAC1 polypeptide or fragment thereof" and determining the functional effect of the compound upon the TRAC1 polypeptide. The recitation "a TRAC1 polypeptide or a **fragment thereof**, the polypeptide or fragment thereof encoded by **a nucleic acid** that hybridizes under stringent conditions to **an antisense** nucleic acid **corresponding** to a nucleic acid encoding **a polypeptide** having **an amino acid sequence** of SEQ ID NO: 1" encompasses virtually any protein. This recitation is interpreted as broadly as is reasonable and as such reads on an

extremely large genus of polypeptides and fragments of polypeptides with no functional limitations and virtually no structural limitations.

The specification, however, only provides the representative species of claimed methods comprising the use of an isolated TRAC1 polypeptide, wherein said TRAC1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1, encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of the necessary TRAC 1 polypeptide by any identifying structural characteristics or properties. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-16 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method comprising contacting a compound (any small organic) with a TRAC1 polypeptide, wherein said TRAC1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1 and determining the functional effect of the compound upon the TRAC1 polypeptide, does not reasonably provide

enablement for any method comprising contacting a compound (any small organic) with any "TRAC1 polypeptide or fragment thereof" and determining the functional effect of the compound upon the TRAC1 polypeptide. As discussed above under the written description rejection and below under the art rejection, the recitation "a TRAC1 polypeptide or a **fragment thereof**, the polypeptide or fragment thereof encoded by **a nucleic acid** that hybridizes under stringent conditions to **an antisense** nucleic acid **corresponding** to a nucleic acid encoding **a polypeptide** having **an amino acid sequence** of SEQ ID NO: 1" encompasses virtually any protein. This recitation is interpreted as broadly as is reasonable and as such reads on an extremely large genus of polypeptides and fragments of polypeptides with no functional limitations and virtually no structural limitations. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-16 and 19 are so broad as to encompass any method comprising contacting a compound (any small organic) with any "TRAC1 polypeptide or fragment

thereof" and determining the functional effect of the compound upon the TRAC1 polypeptide, wherein the "TRAC1 polypeptide encompasses virtually any polypeptide.. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of "TRAC1 polypeptides or fragments thereof" broadly encompassed by the claims. The claims rejected under this section of U.S.C. 112, first paragraph, do not place any functional or structural limits on the recited TRAC1 polypeptides or fragments thereof. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to that method comprising contacting a compound with a TRAC1 polypeptide, wherein said TRAC1 polypeptide comprises the amino acid sequence of SEQ ID NO: 1 and determining the functional effect of the compound upon the TRAC1 polypeptide.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to

modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all methods of use of any TRAC1 polypeptide or modifications and fragments of any TRAC1 polypeptide, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting the desired activity; (B) the general tolerance of TRAC1 polypeptide to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a TRAC1 polypeptide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the desired activity of the TRAC1 polypeptide and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those methods of the claimed genus.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any method comprising contacting a

compound with any "TRAC1 polypeptide or fragment thereof" and determining the functional effect of the compound upon the TRAC1 polypeptide. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those methods of use of those TRAC1 polypeptides, having the desired biological characteristics, is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6-10, 13-16 and 19 are rejected under 35 U.S.C. 102(a) as being anticipated by Sitkovsky (U.S. Patent No. 5,180,662).

Sitkovsky teach methods for the quantitative study of cytotoxic T-lymphocyte activation by measuring secreted granule-associated BLT esterase activity after incubating the cytotoxic T- lymphocytes with activating stimuli. Sitkovsky specifically teach a method comprising contacting a compound with a "TRAC1 polypeptide or a fragment thereof", as defined by the limitations of the claim, and determining the "functional effect" of the compound upon the "TRAC1 polypeptide".

It is acknowledged that the methods taught and claimed by Sitkovsky are not necessarily limited to their use in identifying a compound that modulates T lymphocyte activation or are they limited to the use of the specific embodiments taught by the instant application, however, the methods taught by Sitkovsky anticipate the claimed methods by virtue of the extreme breadth of the claims. For example, applicants claim 1 recites "a TRAC1 polypeptide or a **fragment thereof**, the polypeptide or fragment thereof encoded by **a nucleic acid** that hybridizes under stringent conditions to **an antisense** nucleic acid **corresponding** to a nucleic acid encoding **a polypeptide** having **an amino acid sequence** of SEQ ID NO: 1". This recitation is interpreted as broadly as is reasonable and as such reads on an extremely large genus of polypeptides and fragments of polypeptides with no functional limitations and virtually no structural limitations. Thus the "measuring of secreted granule-associated BLT esterase activity" is considered to be encompassed by "determining the functional effect of the compound upon the TRAC1 polypeptide" (See also above 112 1st and 2nd paragraph rejections).

Claims 15 and 16 are included in this rejection on the basis that, using claim 15 as an example, claim 15 recites "**an** amino acid sequence of SEQ ID NO: 1" and this is interpreted as encompassing **any** amino acid sequence found in SEQ ID NO: 1, for instance, even a di or tri-peptide sequence found within SEQ ID NO: 1.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
11/16/2005